



LUND UNIVERSITY  
DEPARTMENT OF CLINICAL CHEMISTRY  
MALMÖ GENERAL HOSPITAL

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Charles T. Esmon and Naomi L. Esmon  
SERIAL NO: 07/730,040 ART UNIT: 182  
FILING DATE: July 12, 1991 EXAMINER: P. Hutzell  
FOR: MONOCLONAL ANTIBODY AGAINST PROTEIN C  
Commissioner of Patents  
and Trademarks

Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. §1.132

Sir:

I, Johan Stenflo hereby declare that:

1. I am Chairman, Department of Clinical Chemistry, Lund University at Malmö General Hospital, Malmö, Sweden. I received my M.D. at the University of Lund 1968 and my Ph.D. at the same university in 1973. I have conducted research in the area of protein chemistry and hematology since 1969.

2. We have made several sets of monoclonal antibodies against human protein C, even one that is calcium-dependent and unfortunately called HPC-4, just like that of Drs. Esmon. However, our antibody is, of course, entirely different from the HPC-4 of the application and recognizes an epitope in the first EGF-like module.

3. Among the monoclonal antibodies we have made there are several against the activation peptide that do not recognize the active enzyme and, as far as I recall, block activation. However, none of our activation peptide recognizing monoclonal antibodies is calcium dependent.

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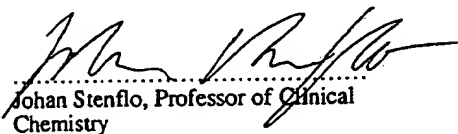
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4. My experience is based on at least four different fusions and we have isolated and characterized at least twenty different stable monoclonal antibodies against protein C.

5. Based on the considerable experience we have of monoclonal antibodies against human protein C and from what I have read in the literature, including Taylor, E. A., J. Clin. Invest., 79:918-925, 1987, Esmon, et al., Develop. Biol. Standard, 67:75-82, 1987 and Stearns, et al., J. Biol. Chem., 263:826-832, 1988, I am convinced that the antibody HPC-4 of the application is truly unique and has very unusual properties which would be difficult, if not impossible to reproduce.

6. I declare that all statements made herein of my own knowledge are true. These statements are made with the knowledge that willful false statements are punishable by fine or imprisonment under applicable laws, and that such willful false statements may jeopardize validity of the application or any patent issuing thereon.

  
Johan Stenflo, Professor of Clinical  
Chemistry

Date: Malmö, Feb 19, 1992